Bad Neighbors

Arsenic-Induced Tumor Cells Convert Normal Stem Cells into a Cancerous Phenotype

Millions of people are exposed to inorganic arsenic, a human carcinogen, in drinking water. *In vitro* and animal studies have shown that malignant cell lines and tumors induced by exposure to inorganic arsenic include more cancer stem cells than other tumor types. Arsenic is known to transform normal stem cells into cancer stem cells, but a new study shows that arsenic-induced malignant cells may do so even without direct arsenic exposure [***EHP* 120(6):865–871; Xu et al.**]. This may explain why arsenic-induced tumors contain so many cancer stem cells.

In normal tissues, stem cells are the source of replacements for damaged or dead cells. Similarly, cancer stem cells are a source of new malignant cells that allow tumors to grow and spread, and they are integral to tumor initiation, progression, and metastasis. The cells' origins and formation are not entirely clear, but evidence suggests they may transform from normal stem cells under the influence of inflammatory cytokines and other factors.

With the prostate identified as a possible target tissue of arsenic, the authors of the current study created malignant epithelial cells (MECs) by exposing a normal human prostatic epithelial cell line, RWPE-1, to sodium arsenite. The RWPE-1 line was also used as the source for normal stem cells, which were co-cultured with either control RWPE-1 cells or MECs. A semipermeable membrane between the cell types in the co-culture system prevented direct cell-to-cell contact but allowed secreted factors to pass freely between cells. The system contained no detectable arsenic.

During the weeks of co-culture and afterward, the investigators assessed the development of a cancer stem cell phenotype, which was defined by the secretion of matrix metalloproteinases (MMPs). Cellular gene expression was assessed at both the transcription and translation levels to determine which factors were involved in the changed phenotype. Finally, normal stem cells cultured alone were treated with interleukin-6 (an inflammatory cytokine secreted by MECs) and then analyzed for MMP activity and gene expression.

Test results indicated that normal stem cells in noncontact co-culture with MECs developed a cancer stem cell phenotype. MMP activity and invasive capacity increased, while *PTEN* tumor suppressor gene expression decreased, similar to previous observations in prostatic cancer stem cells. Changing patterns of gene expression over time, including early loss and later reactivation of several genes, were consistent with changes observed in cancer stem cells during oncogenesis. Similar MMP and gene-expression changes were induced in normal stem cells cultured alone and treated with interleukin-6, suggesting that inflammatory cytokines produced by malignant cells might cause the transformation to cancer stem cells.

The results suggest that MECs may recruit normal stem cells to become cancer stem cells, potentially affecting the growth and spread of cancer, and that interleukin-6 may be one of the recruitment signals. It is unknown whether MECs transformed by carcinogens other than arsenic have a similar ability to alter normal stem cells; more investigation of this mechanism is needed.

Julia R. Barrett, MS, ELS, a Madison, WI–based science writer and editor, has written for *EHP* since 1996. She is a member of the National Association of Science Writers and the Board of Editors in the Life Sciences.

Casting a Wider Net

The Quest for Better Guidance on Seafood Consumption

Fish is the primary dietary source of omega-3 long-chain polyunsaturated fatty acids, which are necessary for healthy prenatal development and linked to reducing cardiovascular disease risk. The type and quantity of seafood that individuals choose to eat can impact both their health and the long-term sustainability of the world's fisheries. An interdisciplinary team of researchers wants consumers to have clearer and more complete guidance in making informed choices about the seafood they eat. Their review presents a framework for producing guidance based not only on nutritional and contaminant information but also ecologic and economic tradeoffs associated with fish consumption choices [***EHP* 120(6):790–798; Oken et al.**].

The review highlights areas of overlap and disagreement in current U.S. guidance regarding what constitutes better choices. The myriad fish consumption advice provided by 21 governmental and nongovernmental entities can leave consumers uncertain how to weigh and reconcile multiple benefits and risks associated with any given fish. For instance, the amount of omega-3 fatty acids provided by different fish varies widely, depending on genetics and diet. And where a fish comes from and what it eats can affect its pollutant load—both wild and farmed fish may be high in toxicants such as methylmercury [also see *EHP* 120(6):799–806; Karagas et al.].

More inclusive fish consumption guides might provide information on ecologic and economic impacts as well as nutritional and contaminant information.

The authors posit that fish consumption advice should reflect the reality that both fish farming and the harvesting of wild fish can profoundly affect the health of the oceans. The annual global fish catch exceeds the maximum sustainable yield by three to four times, and some forms of fishing can devastate ocean ecosystems. Aquaculture, the world's fastest-growing food-production industry, may help ensure adequate fish supplies, but it too has adverse ecological impacts.

The authors recommend that countries develop national lists of fish that can be eaten freely or moderately and fish that should be avoided. These lists should consider all the perspectives analyzed, although the authors acknowledge the challenges of doing so. Ideally, basic national messages would consist of simple lists supplemented by links to more detailed resources for those who desire them, which could be adjusted on a regional basis as necessary. The authors also reaffirm the importance of remediation or elimination of sources of fish contamination as well as policies that promote environmentally responsible and economically viable fishing practices.

Kellyn S. Betts has written about environmental contaminants, hazards, and technology for solving environmental problems for publications including *EHP* and *Environmental Science & Technology* for more than a dozen years.